DNA Photodamage Induced by UV Phototherapy Lamps and Sunlamps in Human Skin *In Situ* and its Potential Importance for Skin Cancer

To the Editor:

Ultraviolet radiation (UVR) from artificial sunlamps has been used for many years to treat skin diseases and to obtain a cosmetic tan at home or in a commercial salon. More than 40 kinds of skin diseases can be treated with artificial UVR by three types of phototherapy, i.e., broadband UVB phototherapy, narrowband UVB phototherapy, and UVA phototherapy (Morison, 1999). Phototherapy combined with some chemicals (e.g., psoralen) (photochemotherapy) is also used to treat certain skin diseases, mainly psoriasis (Lauharanta, 1997; Lowe *et al*, 1997; Morison, 1999). In addition to the phototherapeutic applications, artificial sunlamp use for recreational and cosmetic purposes has become popular in recent years (Oliphant *et al*, 1994; Bulman, 1995; Boldeman *et al*, 1996). No matter which purpose is pursued with artificial UVR, long-term and high dose of exposure is quite common (Diffey, 1990; Miller *et al*, 1998).

UVR is like a double-edged sword with advantages and disadvantages for humans. In addition to the short-term adverse effects after exposure to UVR from sunlamps (e.g., erythema), long-term adverse effects (e.g., photoageing and skin cancer) may also result (Swerdlow and Weinstock, 1998; Morison, 1999). Epidemiologic studies have shown an increased risk for melanoma in sunlamp users (Chen *et al*, 1998; Walter *et al*, 1999; Westerdahl *et al* 2000). These recent studies add to the previous limited evidence on sunlamp use and melanoma (Swerdlow and Weinstock, 1998). It is well known that UVR can induce mutagenic and carcinogenic DNA lesions, mainly cyclobutane pyrimidine dimers (CPD) and 6–4 photoproducts. *In vitro* studies have shown DNA damage in human fibroblasts and keratinocytes after exposure to artificial UVA lamps (Woollons *et al*, 1997, 1999). Yet, direct evidence on DNA damage in human skin after sunlamp applications, which can provide molecular evidence for sunlamp use and skin cancer, is lacking. For this study, we selected two kinds of sunlamps (UVA lamp, Waldmann 85/100w-PUVA, Sylvania, ~1.5% of output at < 315 nm, with maximum peak at 355 nm; UVB lamp, Waldmann 85/100w-UV21, Philips, 0.5% of output < 280 nm, with maximum peak at 315 nm), which are commonly used for the treatment of skin diseases and for tanning purposes, to explore sunlamp-induced DNA damages in human skin *in situ* and its potential importance for skin cancer. The selected doses were automatically administered with a Waldman UV 3003 K sensor calibrated to a distance of 30 cm.

In study I, seven healthy female hospital staff (mean age 43 y) were exposed to clinically frequently used UVR devices (10 J per cm^2 of UVA and 0.2 J per cm^2 of UVB) on the buttock skins. In study II, seven new volunteers (three males and four females, mean age 47 y) were whole body exposed (including the buttock area) to UVA 20 J per cm^2 for 5 d (Monday through Friday). On the following Monday, the treatment was resumed as described. Thus 10 exposures were given. For the skin biopsies a 4 mm diameter punch was used after anesthesization with Xylocain-epinephrine (Astrazeneca, Södertälje, Sweden). All the biopsies were taken within 10 min after irradiation and were immediately put on dry ice, frozen, and stored at –20°C until DNA isolation. In study II, the biopsies were taken on Fridays after the fifth and tenth irradiation, respectively. Preirradiation biopsies were taken as controls.

The ^{32}P-postlabeling method was used to quantify the photoproduct levels in epidermal DNA as described (Bykov and Hemminki, 1995; Xu *et al* 2000). The photoproducts were assayed as a trinucleotide with an unmodified nucleotide at the 5′-side. In this study, four kinds of photoproducts were determined, TT=C, TT=T as CPDs and TT-C, TT-T as 6–4 photoproducts. Each sample was analyzed twice.

There were no detectable photoproducts in any of the preirradiation skin biopsies, so only data on UVR-exposed samples were presented. We defined the level as undetectable when the signal of the relevant fraction did not reach two times that of the background noise levels in HPLC chromatography.

Irradiation with 10 J per cm^2 UVA or 0.2 J per cm^2 UVB induced photoproducts in human skin *in situ* (**Table I**). The UVB lamp was much more efficient than the UVA lamp at the doses used. TT=T was more abundant than TT=C but the relative proportion of these were different after UVA and UVB, 3.4 after UVA and 2.1 after UVB (**Table I**). The relative proportion of TT=T to TT-T changed even more depending on the UV source (**Table I**).

Irradiation with 20 J per cm^2 of UVA per day for 5 or 10 d induced photoproducts at levels higher than those observed after a single exposure on different subjects (**Table II**); however, comparison of photoproduct levels produced after the fifth and the tenth UVA exposure showed no large difference ($p > 0.05$) (**Table II**).

In this study, two UV lamps commonly used for dermatologic treatment and tanning purposes were selected to assess DNA damage in human skin *in situ*. It was clearly shown that UV lamps could induce detectable DNA damage in the sunlamp user's skin *in situ* for both phototherapeutic and cosmetic applications (**Tables I** and **II**). Irradiation with the UVB lamp induced more DNA damage than with the UVA lamp. This is not surprising because DNA absorbs more UV radiation in the UVB range than in the UVA range (IARC, 1992). In phototherapy, both UVB and UVA are used (Jekler and Larko, 1990, 1991a, ,b). For those whose disease is suitable for UVB treatment, both the UVB dose and the number of treatments should be taken into account due to much more DNA damage induced by UVB lamp.

It is known that photoproducts are mutagenic and probably carcinogenic and that they are slowly repaired in the p53 mutation hotspots for skin cancer (Tornaletti and Pfeifer, 1994). Assuming that these UV lamps are used in sun parlors, enormous DNA damage would be expected in users' skin. A frequent sunlamp tanner (100 sessions per year, Miller *et al*, 1998) will produce 100 times higher cumulative amounts of CPD in skin than a single

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Table I. UVB lamp was more efficient to induce DNA photodamage than UVA lamp in human skin *in situ*

	TT=C (n=7)	TT=T (n=7)	TT-C (n=7)	TT–T (n=7)	TT=T/TT=C	TT=T/TT–T	TT=C/TT–C
10 J per cm^2 UVA	1.15±0.25	3.92±0.72	0.34±0.11	0.17±0.08	3.41	23.06	3.38
0.2 J per cm^2 UVB	17.82±2.02*	37.52±5.03*	4.31±0.53*	4.25±0.44*	2.10	8.83	4.13

[a]Mean±SD, per 10^6 Nt; study I.
Nt, nucleotide. *Differences in photoproduct levels after 0.2 J per cm^2 UVB and 10 J per cm^2 UVA irradiation were analysed by Student's *t* test, $p<0.01$.

Table II. Repetitive UVA irradiation induced DNA photodamages in human skin *in situ*

	TT=C (n=7)	TT=T (n=7)	TT-C (n=7)	TT–T (n=7)	TT=T/TT=C
20 J per cm^2 UVA (×5 d)	2.58±0.83	10.20±2.76	0.16±0.17	0.21±0.21	3.95
20 J per cm^2 UVA (×10 d)	2.12±0.59	10.97±2.82	0.17±0.29	0.51±0.38	5.17

[a]Mean±SD, per 10^6 Nt; study II.
Nt, nucleotide.

UVA lamp exposure (10 J per cm^2) and five times more than a typical sunlamp tanner (20 sessions per year, Miller *et al*, 1998). During the treatment for psoriasis with a UVB lamp (20 exposures, IARC, 1992), the patient will receive 20 times higher cumulative amounts of CPD than in a single UVB lamp exposure (0.2 J per cm^2). Epidemiologic studies have shown that the increased risk in skin cancer (both melanoma and nonmelanoma) is related to UVR exposure during tanning and psoriasis treatment (Chen *et al*, 1998; Frentz *et al*, 1999; Walter *et al*, 1999; Hannuksela-Svahn *et al* 2000; Westerdahl *et al* 2000). The vast amounts of DNA damage induced during chronic sunlamp use, if unrepaired, will increase the possibility of tumorigenesis in skin. Our results showed biologic plausibility at the molecular level for possible carcinogenic effects of sunlamp applications.

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